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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/582,982
Filing Date: June 15, 2006
Appellant(s): SHIPMAN ET AL.

Courtenay Brinckerhoff
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/19/2009 appealing from the Office action mailed March 30, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Denefle et al (WO02/46458, published June 13, 2002)

Dean et al (Journal of Lipid Research (2001) volume 42, pages 1007-1017)

Monahan et al (WO2/071928 published 19 September 2002)

Schmitz (WO00/18912 Published April 6, 2000)

GenBank accession AC069137.6 GI:14589784 Published July 3, 2001)

Boyd et al (WO01/62977 published August 21, 2001)

Gen Bank Accession U63970.1 GI:1764161 (published Jan 7, 1997)

Wan et al (WO2002/74979, published September 26, 2002)

Kruh et al (WO99/49735 published Oct 7, 1999)

GenBank Accession Z31010.1 GI:479155 (published May 11, 1995)

Ota et al (EP1074617A2 published 07.02.2001)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 49, 50 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Denefle et al (WO02/46458, published June 13, 2002) in view of Dean et al (Journal of Lipid Research (2001) volume 42, pages 1007-1017); Monahan et al (WO2/071928 published 19 September 2002) (only relevant pages were provided due to length of disclosure); Schmitz (WO00/18912 PUBLISHED April 6, 2000); GenBank accession AC069137.6 GI:14589784 Published July 3, 2001); Boyd et al (WO01/62977 published August 21, 2001); Gen Bank Accession U63970.1 GI:1764161 (published Jan 7, 1997); Wan et al (WO2002/74979, published September 26, 2002) (only relevant pages were provided due to length of disclosure); Kruh et al (WO99/49735 published Oct 7, 1999); GenBank Accession Z31010.1 GI:479155 (published May 11, 1995); Ota et al (EP1074617A2 published 07.02.2001) (only relevant pages were provided due to length of disclosure).

Denefle teaches characterization of new ABC genes will yield important transporter genes (see page 3, lines 27-29). Denefle teaches, "Thus, the probes according to the invention, immobilized on a support, may be ordered into matrices such as "DNA chips". Denefle thus teaches a microarray of ABC transporter genes.

Denefle does not teach probes consisting of SEQ ID NO 12, 15, 21, 22, 23, 24, 25, 26, 35, and 44. Denefle does not suggest the combination of probes of SEQ ID NO 12, 15, 21, 22, 23, 24, 25, 26, 35, and 44.

However, Dean et al teaches the ABC transporter family comprises 48 known ATP driven transporters, which have numerous important biological functions (see page 1007). Dean teaches the ABC family genes are known to play a role in the cell and

mutations in the ABC gene transporter have been found in cystic fibrosis, neurological disease, retinal degeneration, cholesterol and bile transport defects, anemia, and drug response.

Monahan teaches sequence ABS76368 which comprises nucleotides of 3781 to 4570 are identical to SEQ ID NO 12.

Schmitz et al teaches AAZ94742 which comprises nucleotides 3082-3871 are identical to SEQ ID NO 15.

GenBank accession AC069137.6 GI:14589784 teaches nucleotides 93414 to 92662 comprising SEQ ID NO 21 of instant invention.

Boyd WO0162977 teaches GenBank accession AX282509.1 GI:16609639 nucleotides 21344 to 22003 which comprise SEQ ID NO of instant invention.

Gen Bank Accession U63970.1 GI:1764161 teaches nucleotides 4011-4820 which comprise the nucleotides of SEQ ID NO 23.

Wan teaches sequence ABZ35350 nucleotides 4566 to 5286 which comprises SEQ ID NO 24 of instant invention.

Kruh et al teach sequence AAZ30078 nucleotides 3336 to 4129 which comprises SEQ ID NO 25 of instant invention.

Kruh et al teach sequence AAZ30079 nucleotides 4964 to 5069 which comprises SEQ ID NO 26 of instant invention.

GenBank Accession Z31010.1 GI:479155 teaches nucleotides 1280 to 1767 which comprise SEQ ID NO 35 of instant invention.

Ota et al (EP1074617A2 published 07.02.2001) teaches SEQ ID NO 12961 nucleotides 1387 to 2010 which comprise SEQ ID NO 44 of instant invention.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequences taught by Monahan et al, Schmitz, GenBank accession AC069137.6 GI:14589784, Boyd et al, Gen Bank Accession U63970.1 GI:1764161, Wan et al, Kruh et al, GenBank Accession Z31010.1 GI:479155, and Ota et al which comprise SEQ ID NO 12, 15, 21, 22, 23, 24, 25, 26, 35, 44 in the array taught by Denefle. Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes. As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific SEQ ID NO 12, 15, 21, 22, 23, 24, 25, 26, 35, 44 and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from the known sequences. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations. The artisan would be

motivated to combine the nucleic acid sequences taught by Monahan et al, Schmitz, GenBank accession AC069137.6 GI:14589784, Boyd et al, Gen Bank Accession U63970.1 GI:1764161, Wan et al, Kruh et al, GenBank Accession Z31010.1 GI:479155, and Ota et al because Dean teaches ABC gene transporters are important and known to play a role in human diseases including cystic fibrosis, neurological disease, retinal degeneration, cholesterol and bile transport defects, anemia, and drug response, thus determining expression would allow better diagnosis. The substitution or addition of the sequences taught by Monahan et al, Schmitz, GenBank accession AC069137.6 GI: 14589784, Boyd et al, Gen Bank Accession U63970.1 GI: 1764161, Wan et al, Kruh et al, GenBank Accession Z31010.1 GI: 479155, and Ota et al in the arrays taught by Denefle would produce a microarray with probes equivalent to the recited SEQ ID NO by replacing or adding known ABC transporter gene sequences for another. The artisan would have a reasonable expectation of success as methods of synthesizing nucleic acids and making arrays as well as the sequences of ABC transporter genes were known at the time of the invention.

(10) Response to Argument

The instant invention is drawn to a microarray comprising probes for the detection ABC transporter genes as the brief indicates. As disclosed in the rejection under appeal sequences comprising all the claimed SEQ ID NO were known at the time of filing. The examiner has presented the rejection and noted that the claims are obvious absent secondary considerations. While applicant has presented a declaration asserting secondary considerations in selection of the probe sequences, the claims are

drawn to a product having nucleic acid sequences. The declaration thus does not demonstrate an unexpected result or secondary consideration of the claimed product.

The brief begins by noting, "At the outset, Appellants note their disagreement with the Examiner's interpretation of the transitional phrase "having," explained in the Advisory Action dated September 20, 2009 ("Advisory Action"). The Examiner maintains that the "use of the broad 'have' followed by the narrow 'consisting of' results in a broad claim interpretation." Advisory Action at 5. Appellants disagree. As stated in MPEP § 2111.03, "[t]ransitional phrases such as 'having' must be interpreted in light of the specification to determine whether open or close language is intended." Moreover, the same section of the MPEP cites to Crystal Semiconductor Corp. v. TriTech Microelectronics Int'l., Inc., 246 F.3d 1336, 1348 (Fed. Cir. 2001), for the proposition that the "term 'having' in transitional phrase 'does not create a presumption that the body of the claim is open.'" Indeed, the Federal Circuit in Crystal Semiconductor states that "the term 'having' does not convey the open-ended meaning as strongly as 'comprising.'" Id. Claim 49 recites that "at least two of the nucleic acid molecules have a nucleic acid sequence consisting of SEQ ID NO: 12, 15, 21 .... " In this context, it is clear that the term "have" is intended to be a closed term." These arguments have been thoroughly reviewed but are not considered persuasive as MPEP2111.03 further cites Lampi Corp. v.American Power Products Inc., 228 F.3d 1365, 1376, 56 USPQ2d 1445, 1453 (Fed. Cir. 2000) (The term "having" was interpreted as open terminology, allowing the inclusion of other components in addition to those recited); Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1573, 43 USPQ2d 1398, 1410 (Fed. Cir.

1997) (In the context of a cDNA having a sequence coding for human PI, the term "having" still permitted inclusion of other moieties.). Thus as the specification does not present a limiting definition of "having" the broadest reasonable interpretation is "comprising" or open language.

The brief continues by asserting that the specification discloses probes on an array that are less than 900 nucleotides in length and that full length ABC transporter genes sequences are not suitable for use as probes on an array. First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the probes of full length ABC transporter genes not being suitable for use as probes on an array are arguments of counsel that have not been supported by any evidence. Further the teachings of Denefle teaches that nucleotide sequences of 1000 to 1500 consecutive nucleotides can be used as probes or nucleic acids comprising SEQ ID NO 1-4 and 9-126 of Denefle disclosure. Thus the assertion that probes of greater than 900 nucleotides in length are not suitable for use as probes is not persuasive.

The brief continues by asserting that the Final action of March 30, 2009 does not make a prima facie case of obviousness as the art of record does not teaches probes consisting of the claimed nucleotide sequences. These arguments have been thoroughly reviewed but are not considered persuasive as the prior art of record teaches the sequences were known, suggests making microarrays, and provides motivation to produce microarrays to examine ABC transporter gene expression of probes that are functional equivalents to those claimed.

The brief continues by noting, "As taught in the specification, the recited probes are useful for uniquely identifying nucleic acid molecules that encode different human ABC transporters. Denefle is cited for teaching that the "characterization of new ABC genes will yield important transporter genes," and that its probes can be "immobilized on a support,... [and] ordered into matrices such as 'DNA chips.'" Final Office Action at 5. Dean is cited for teaching that "the ABC transporter family comprises 48 known ATP driven transporters, which have numerous important biological functions." Id. at 6. The other references are cited for teaching full-length ABC transporter gene sequences, including genomic sequences, that comprise the sequences of probes recited in the claims (i.e. SEQ ID NOs: 12, 15, 21, 23, 24, 25, 26, 35 and 44). The Final Office Action asserts that it would have been obvious to use the prior art sequences in the array of Denefle, and that "[t]he artisan would be motivated to combine the [prior art] sequences.., because Dean teaches ABC gene transporters are important." Id. at 8. According to the Final Office Action, "the substitution or addition of the [prior art] sequences.. would produce a microarray with probes equivalent to the recited SEQ ID

NO." The response appears to be alleging that Denefle and Dean do not suggest making an array to examine the expression of ABC transporter genes. These arguments have been thoroughly reviewed but are not considered persuasive as the claims are drawn to a product of an array and thus are examined by their structural features not their intended use as asserted. Further, Denefle teaches on page 50 determination of expression of ABCA9, ABCA5, and ABCA6, thus suggesting determining expression levels.

The brief continues by asserting one of skill in the art would not be motivated to make an array for detection of ABC transporter expression contrary to the assertion of the rejection. These arguments have been thoroughly reviewed but are not considered persuasive as Dean teaches, "analysis of ABC gene expression combined with gene disruptions should yield important clues to gene function" (page 1165, 1st column last paragraph), while Denefle suggests the making of microarrays, thus rendering obvious to one of skill in the art making a microarray to detect ABC transporter gene expression.

The brief asserts the cited references provide no guidance or motivation to make an array containing the claimed nucleic acids which are capable of simultaneously distinguishing between members of human ATP binding cassette transporter gene family. The brief further notes the claims are not drawn to individual oligonucleotides by a combination of sequences that each specifically hybridizes to an individual ABC transporter gene. These arguments have been thoroughly reviewed but are not considered persuasive as claim 49 is drawn to at least two nucleic acid molecules that are immobilized on a substrate and thus the arguments are beyond the scope of the

invention of claim 49. Further the claims are drawn to, "a probe that specifically hybridizes to a sequence encoding a human ABC transporter" gene. While this encompasses probes that hybridize to a single nucleic acid it does not require it, as the specification defines specifically hybridizes to include" hybridize substantially to or only with a particular nucleic acid sequence with minimum cross-hybridization with the other members of this gene family" (page 16, lines 5-10). Further recitation of specifically hybridizes encompass any hybridization conditions and one of skill in the art could modify hybridization conditions to allow a single sequence to hybridize to a single probe. Finally, in the presence of a sample with a single ABC transporter gene the probes would specifically hybridize to the single transporter in the sample.

The brief further asserts, "Because the cited references are wholly lacking any teaching or guidance that would have led the skilled artisan to the claimed invention, and do not provide any motivation or reason to select the recited sequences, the obviousness rejection is improper and should be withdrawn." These arguments have been thoroughly reviewed but are not considered persuasive as Dean teaches, "analysis of ABC gene expression combined with gene disruptions should yield important clues to gene function" (page 1165, 1st column last paragraph), while Denefle suggests the making of microarrays, thus rendering obvious to one of skill in the art making a microarray to detect ABC transporter gene expression.

The brief continues by asserting that the full length prior art sequences do not render the instant specific probes obvious. These are arguments of counsel that have not been substantiated by evidence. It is noted that MPEP 2183 states a prima facie

obvious case of equivalence can be made if the prior art elements perform the function of the claim, is not excluded by a specific definition and is an equivalent of a means (or step) plus function limitation. MPEP 2183 directs applicants that non-equivalence can be shown by the specification teaching the prior art is not an equivalent, a teaching of the prior art reference itself showing non-equivalence, or a declaration under 37 CFR1.132 showing evidence of non-equivalence. Neither the brief nor previous responses have shown that the prior art or specification demonstrate non-equivalence of probes based on the prior art knowledge of the full length sequences. The declaration provided is drawn to methods of selecting the probes and has not provided any evidence that probes derived from the known sequences would not function in an equivalent fashion to those claimed.

The brief then presents several, "unpublished" Board decisions to support their assertion of non-obviousness. It is noted that Board decision relied upon by applicant have not been determined to be precedential or informative decision of the board and thus do not precedent for examination or appeals.

The brief first provides the decision of Ex parte Bandman, which the brief indicates "undefined probes" are obvious over a full length sequence. First the instant claims are drawn to an array or product, while the Bandman appeal is directed to method claims. Thus the fact pattern of Bandman is not consistent with the instant product claim.

The brief then present Ex Parte Kolberg to support their position of non-obviousness. In Ex parte Kolberg there is evidence of an unexpected resulted

(radiation sensitivity of a promoter). In the instant case the specification and arguments of record provide no unexpected results.

The response then argues in Re O'Farrell and Kubin. These arguments have been thoroughly reviewed but are not considered persuasive as the Denefle teaches probes that would function to allow detection of ABC transporter genes as the response asserts is the intended use of the claimed invention. Further the examiner has provided specific sequences and motivation to combine them in an array. There is no evidence that the combined teachings result in anything more then the predictable use of prior art elements according to their established function.

The brief on page 18 then asserts, "There is no evidence that such an array would be functionally equivalent to the claimed array. As set forth above, the claimed arrays comprise probes that each uniquely identify a single ABC transporter gene out of a family of at least 48 human ABC transporter genes known at the time of filing. There is no evidence that the sequences in the art, which include full-length, genomic sequences, could perform this function. Indeed, such full-length sequences would not be suitable for use as probes on an array because of their length." These arguments have been thoroughly reviewed but are not considered persuasive as first they are arguments of counsel that have not been substantiated by evidence as there is no evidence that the full length sequences could not work, while Denefle specifically suggests the use of longer sequences as probes. MPEP 2183 directs applicants that non-equivalence can be shown by the specification teaching the prior art is not an equivalent, a teaching of the prior art reference itself showing non-equivalence, or a

declaration under 37 CFR1.132 showing evidence of non-equivalence. Neither the brief nor previous responses have shown that the prior art or specification demonstrate non-equivalence of probes based on the prior art knowledge of the full length sequences. The declaration provided is drawn to methods of selecting the probes and has not provided any evidence that probes derived from the known sequences would not function in an equivalent fashion to those claimed.

Second, the rejected claims do not specifically require probes that "uniquely identify" a single ABC transporter gene. Claim 48 and 49 provide no limitations as to the specificity of the probes, while claim 78 is drawn to probes that "specifically hybridize" to human ABC transporter genes, under any conditions including a hybridization assay in which a single ABC transporter gene is present in the hybridization solution. The recitation of "specifically hybridized" as defined in the instant specification allows for some cross hybridization and thus does not require the probe uniquely identify a single ABC transporter gene as asserted in the brief. Further the probes would specifically hybridize a single ABC transporter gene under highly stringent conditions if only a single ABC transporter gene was present in the hybridization solution.

The response then moves to another non-precedential Board decision of Ex Parte Weichselbaum. The decision appears to rely upon ambiguity by the examiner as to what equivalent coding sequences are in the Ex parte Weichselbaum. However, in the instant case the sequences for the claimed ABC transporter genes are known and the final rejection states, "Designing probes, which are equivalents to those taught in

the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes. As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific SEQ ID NO 12, 15, 21, 22, 23, 24, 25, 26, 35, 44 and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from the known sequences. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations. The artisan would be motivated to combine the nucleic acid sequences taught by Monahan et al, Schmitz, GenBank accession AC069137.6 GI:14589784, Boyd et al, Gen Bank Accession U63970.1 GI:1764161, Wan et al, Kruh et al, GenBank Accession Z31010.1 GI:479155, and Ota et al because Dean teaches ABC gene transporters are important and known to play a role in human diseases including cystic fibrosis, neurological disease, retinal degeneration, cholesterol and bile transport defects, anemia, and drug response, thus determining expression would allow better diagnosis. The substitution or addition of the sequences taught by Monahan et al, Schmitz, GenBank accession AC069137.6 GI: 14589784, Boyd et al,

Gen Bank Accession U63970.1 GI: 1764161, Wan et al, Kruh et al, GenBank Accession Z31010.1 GI: 479155, and Ota et al in the arrays taught by Denefle would produce a microarray with probes equivalent to the recited SEQ ID NO by replacing or adding known ABC transporter gene sequences for another. " Thus there is no such ambiguity in the instant rejection.

The brief on page 19 asserts that the doctrine of functional equivalence cannot be relied upon in the instant rejection. The response then presents arguments From MPEP 2144.06 to equivalents known for the same purpose and cites, " In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents." 2144.06 continue to place this statement in context by teaching, "The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components." The instant rejection is not based on the presence of the nucleotide sequences in a Markush group, but the determination that the sequences were known and part of a known gene family of interest. Further the nucleic acid sequences of the gene can function as probes and methods of making probes was known, absent secondary considerations.

The response continues by asserting that no prior art arrays or probes have been identified. These arguments have been thoroughly reviewed but are not considered persuasive as Denefle teaches, "According to a specific embodiment of the detection kit described above, such a kit will comprise a plurality of oligonucleotide probes and/or

primers in accordance with the invention which may be used to detect a target nucleic acid of interest or alternatively to detect mutations in the coding regions or the non-coding regions of the nucleic acids according to the invention, more particularly of nucleic acids comprising any one of SEQ ID NOs: 1-4 and 9-126, or a complementary nucleotide sequence. Thus, the probes according to the invention, immobilized on a support, may be ordered into matrices such as "DNA chips". Such ordered matrices have in particular been described in US patent No. 5,143,854, in published PCT applications WO 90/15070 and WO 92/10092. Support matrices on which oligonucleotide probes have been immobilized at a high density are for example described in US patent No. 5,412,087 and in published PCT application WO 95/11995." (bottom page 68-top page 69). Further Denefle teaches the probes of the invention can be used to detect target nucleic acids (page 70, lines 25-27). Further the teachings of Denefle teaches that nucleotide sequences of 1000 to 1500 consecutive nucleotides can be used as probes or nucleic acids comprising SEQ ID NO 1-4 and 9-126 of Denefle disclosure. Further Monahan suggests the use of marker nucleic acids attached to a substrate (page 34), thus suggesting probes and arrays. Further Schmitz teaches the use of probes for ABC1 and ABC8 (page 30), thus demonstrating probes were known. Further Wan suggests the use of microarrays in the detection of the sequences in a gene expression profile, thus demonstrating the use of probes and arrays to ABC transporter genes were known (page 4). Further, Kruh teaches the use of probes to detect ABC transporter genes on a blot.

It is noted that MPEP 716.02 is drawn to declaration or affidavits demonstrating an unexpected results, which appears to be the criteria applicant's are relying upon to differentiate the claimed arrays from the prior art of record. The brief continues, "this rejection places Appellants in the impossible position of needing to establish that the claimed arrays of probes are not functionally equivalent to fictional probes, whose specific properties and functions cannot be ascertained, tested or compared. Indeed, MPEP § 716.02(e) expressly states that "applicant is not required to compare the claimed invention with subject matter that does not exist in the prior art" (emphasis added)." These arguments have been thoroughly reviewed but are not considered persuasive as the prior art discloses sequences comprising the claimed SEQ ID NO were known. The prior art further suggests or uses the prior art sequences as probes, thus the rejection relies on prior art teachings which do exist contrary to the assertion of the brief. Further the prior art suggests the use of probes to ABC transporters on microarrays.

The brief continues by asserting the examiner is requiring applicant to compare the claimed invention to prior art that does not exist. The response asserts that no specific array of ABC transporter genes is present in the prior art. As described in the final rejection and above the cited references disclose sequences comprising the claimed sequences, suggest making a microarray for detection of ABC transporter genes and provides motivation for arrays detecting expression of all ABC transporter genes. Thus the prior art does exists.

The brief continues by noting the declaration by Dr. Shipman attempts to address the issue in a declaration in which the inventor provides a bioinformatic approach based on primer design software. The response asserts, "In performing this analysis, Dr. Shipman used information that would not have been available to the skilled artisan without knowledge of the present application, such as the target PCR product sizes which Dr. Shipman set to correspond to the size of the claimed probes.... the program did not identify the claimed probe sequences or even sequences that were equivalent thereto. As Dr. Shipman explains, the data obtained indicate that the claimed probes would be better at identifying their targets under stringent conditions than the comparison probes." These arguments have been thoroughly reviewed but are not considered persuasive as the declaration has provided no evidence that the probes function better under stringent conditions, but merely provide a computer based analysis. The declaration notes at point 19 that in silico analysis of DNA sequences is not predictable providing a single PCR product, thus attesting to the unpredictability of such analysis. Thus applicant has asserted that the claims have improved results based on in silico analysis in while noting the in silico analysis is not predictable. Further, the declaration states, In all cases, sequences selected using computer programs need to be verified and validated and in almost all cases, the experience, knowledge and skill of a senior scientist is required to obtain a sequence that, when reduced to practice, provides the desired probe product and performance in gene expression analyses." Again, the declaration suggests the unpredictability of such analysis.

The response continues by asserting, "The Examiner alleges that the Declaration is not persuasive because, allegedly, the skilled artisan would have undertaken the same steps that the present inventors took to arrive at the present invention, e.g., the same verification, validation and selection steps. See Final Office Action at 3. This assertion is made without any support whatsoever, and again leaves Appellants tilting at windmills, because the record is simply devoid of any evidence of any motivation that would have led a skilled person to even attempt to design an array as claimed, let alone any of the parameters that might have guided such an undertaking. To the contrary, Dr. Shipman attested that "the prior art does not teach the necessary information that would allow a person skilled in the art to identify probe sequences such as the specific nucleic acid sequences found in the Application." These arguments have been thoroughly reviewed but are not considered persuasive as the final rejection and above the cited references disclose sequences comprising the claimed sequences, suggest making a microarray for detection of ABC transporter genes and provides motivation for arrays detecting expression of all ABC transporter genes.

The brief then asserts the instant invention cannot be considered "obvious to try." The response asserts, " there is a very large number of possible probes for each of the 48 genes, because the probes can be of widely different lengths and can be chosen from different regions of the gene. The number of possibilities increases exponentially when designing an array, because one of skill in the art making an array could chose any probe for one gene to use with any probe for another gene, etc. Even if there were only 10 possible probes for each gene, that would result in 1×10^{48} possible arrays.

Focusing on the 10 probes recited in the claims, and assuming only 10 possible probes for each gene, the claimed array is still 1 out of a possible 10,000,000,000. This is a far cry from the finite number of "identified and predictable solutions" required by KSR. In Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1359 (Fed. Cir. 2007), the court emphasized that obviousness requires that the prior art give a reason or motivation to make the specific composition claimed." These arguments have been thoroughly reviewed but are not considered persuasive as the instant rejection is not based on the obvious to try rationale, but based on substitution of functional equivalents. Further, claim 49 is drawn to two or more probes, while claim 78 requires 10 probes, thus the claims do not require probes to the 48 genes, and thus the arguments are beyond the scope of the claimed invention. The response supports this argument by use of Takeda Chemical Industries, Ltd V. Alphapharma Pty, ltd 492 F3d 1350, 1350 Fed Circ 2007) and asserts that the court emphasized the obviousness requires a reason or motivation to make a specific compound. These arguments have been thoroughly reviewed but are not considered persuasive as the prior art suggests the making of an array and probes to detect expression of ABC transporter genes. The full length sequences of the ABC transporter genes of the prior art of record would function as probes on microarrays, thus the teachings of the prior art provide motivation to make probes that are functionally equivalent.

In conclusion, the instant invention is drawn to a microarray comprising probes for the detection ABC transporter genes as the brief indicates. As disclosed in the rejection under appeal sequences comprising all the claimed SEQ ID NO were known at

the time of filing. The examiner has presented the rejection indicating that the prior art taught sequences comprising the claimed SEQ ID NO, suggested the use of microarrays for detection of ABC transporter expression and provided motivation for detecting ABC transporter sequences. The examiner noted that the claims are obvious absent secondary considerations. While applicant has presented a declaration asserting secondary considerations in selection of the probe sequences, the claims are drawn to a product having nucleic acid sequences. The declaration thus does not demonstrate an unexpected result or secondary consideration of the claimed product.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Steven C Pohnert/

Examiner, Art Unit 1634

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